Criteria for Non-formulary Use of Insulin Glargine (Lantus®)

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These criteria were developed using the best evidence currently available. The following recommendations are dynamic and will be revised, as new clinical data become available. These guidelines are not intended to interfere with clinical judgment. Rather, they are intended to assist practitioners in providing consistent, high quality cost effective care.

1. Insulin glargine was approved April 2001, for type 1 and 2 diabetes. It is the first long-acting insulin analog that provides consistent insulin levels over a 24-hour period without a significant peak effect.

Criteria for VA use

- Insulin glargine is not recommended for insulin naïve patients.

- Patients unable to achieve glycemic control targets because of recurrent episodes of symptomatic hypoglycemia, especially with nocturnal hypoglycemia, despite multiple attempts with various insulin dosing regimens.

OR

- Patients receiving highly intensive insulin therapy such as 4 times daily administration including those who would otherwise be candidates for insulin pump therapy. *

AND

- The prescriber must document improvement in either glucose control or hypoglycemia during the first 6 months of treatment. If no improvement is noted, insulin glargine should be discontinued.

* This recommendation is based on the pharmacokinetic/pharmacodynamic profile of glargine which suggest a more steady insulin level and which may assist patients who are trying to maintain very strict and tight control of their blood sugar while minimizing symptomatic hypoglycemia.

2. **Summary of comparative efficacy trials (abstracts excluded)**

Type 1 diabetes

- NPH and glargine have been compared in 4 clinical trials (2 were 4 weeks, 1 was 16 weeks, and 1 was 28 weeks in duration).
- Patients had mean baseline HbA1c around 7.8%
- Fasting blood glucose decreased by 14-27mg/dL (range of means from the 4 studies) over that of NPH. Fasting plasma glucose decreased by 30-50mg/dL over that of NPH. In the 2 longer-term studies, HbA1c did not differ at endpoint between the insulin glargine versus the NPH groups.
- 2 out of the 4 studies showed a lower incidence of nocturnal hypoglycemia with insulin glargine (36% vs. 56%: 18% vs. 27%). Overall symptomatic hypoglycemia was lower with insulin glargine in one study (40% vs. 49.2%)
- More injection reactions were seen with insulin glargine.

Type 2 diabetes

- Two long-term studies evaluated insulin glargine and NPH in type 2 DM. One study assessed adding glargine to previous oral agent(s). The second study assessed type 2 diabetics who were receiving only insulin.
- Patients had a mean baseline HbA1c ranging from 8.5-9.1%
- In both studies, patients achieved similar glucose control regardless of whether they received insulin glargine or NPH.

- Insulin glargine patients had a lower incidence of nocturnal hypoglycemia (10% vs. 23%; 31.3% vs. 40.2%). Overall, symptomatic hypoglycemia was lower with insulin glargine in one study (33% vs. 42%).

3. **Safety issues**

Three-grade progression of retinopathy was observed in 7.5% of subjects with type 2 diabetes treated with insulin glargine for 1 year or less compared to 2.7% observed in the NPH group. An independent panel convened by Aventis concluded that this finding was not related to insulin glargine. The FDA, in its letter of approval, has asked Aventis to commit to a phase IV trial to look at the proportion of type 2 patients who have a three-step or more progression of retinopathy during treatment with insulin glargine or NPH.

Insulin glargine has 6-fold greater affinity for insulin-like growth factor I (IGF-1) receptor than human insulin. In cell-lines expressing a high number of IGF-1 receptors (eg. human osteosarcoma cell line Saos/B10 and human mammary epithelial cells), a relation between IGF-1 receptor affinity and mitogenic potential has been described. However, insulin glargine administered to rats in doses of 2-12U/kg for 2 years did not have a carcinogenic effect. The clinical relevance of this is unknown; however, the European Agency for the Evaluation of Medicinal Products has issued a draft concept paper asking the manufacturer to define appropriate procedures for the non-clinical assessment of carcinogenic potential of human insulin analogues.

There are no well-controlled studies using insulin glargine in pregnant or nursing women; therefore, it should be avoided unless clearly needed.

4. **Dosing**

Switching from NPH to insulin glargine

- Patients on NPH once daily - may be switched unit-for-unit to insulin glargine once daily at bedtime
- Patients on NPH twice daily – total glargine dose should be approximately 80% of the previous NPH dose and should be given once daily, at bedtime.

Insulin glargine is a clear solution and must not be mixed with any other insulin. Doing so can alter the pharmacokinetic/pharmacodynamic profile making the action of insulin glargine unpredictable.

References

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